Acta Biomaterialia 8 (2012) 3606–3617

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Differential functional effects of biomaterials on dendritic cell maturation

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ARTICLE INFO

Article history:
Received 28 December 2011
Received in revised form 1 June 2012
Accepted 6 June 2012
Available online 12 June 2012

Keywords:
Biocompatibility
Immunomodulation
Dendritic cells
Biomaterials
Combination products

ABSTRACT

The immunological outcome of dendritic cell (DC) treatment with different biomaterials was assessed to demonstrate the range of DC phenotypes induced by biomaterials commonly used in combination products. Immature DCs (iDCs) were derived from human peripheral blood monocytes, and treated with different biomaterial films of alginate, agarose, chitosan, hyaluronic acid (HA), or 75:25 poly(lactic-co-glycolic acid) (PLGA) and a comprehensive battery of phenotypic functional outcomes was assessed. Different levels of functional changes in DC phenotype were observed depending on the type of biomaterial films used to treat the DCs. Treatment of DCs with PLGA or chitosan films supported DC maturation, with higher levels of DC allostimulatory capacity, pro-inflammatory cytokine release, and expression of CD80, CD86, CD83, HLA-DQ and CD44 compared with iDCs, and lower endocytic ability compared with iDCs. Alginate film induced pro-inflammatory cytokine release from DCs at levels higher than from iDCs. Dendritic cells treated with HA film expressed lower levels of CD40, CD80, CD86 and HLA-DR compared with iDCs. They also exhibited lower endocytic ability and CD44 expression than iDCs, possibly due to an insolubilized (cross-linked) form of high molecular weight HA. Interestingly, treatment of DCs with agarose film maintained the DC functional phenotype at levels similar to iDCs except for CD44 expression, which was lower than that of iDCs. Taken together, these results can provide selection criteria for biomaterials to be used in immunomodulating applications and can inform potential outcomes of biomaterials within combination products on associated immune responses as desired by the application.

1. Introduction

In tissue engineering applications immune responses should be minimized, whereas vaccine strategies aim to enhance the protective immune response. Adjuvants enhance an immune response by interacting with antigen-presenting cells (APCs) such as dendritic cells (DCs) during the innate immune response which, upon maturation, bridge the innate and adaptive immune response by stimulating T lymphocytes. Hence, the adjuvant effect of biomaterials can be determined by assessing their effect on the maturation of DCs.

Biomaterial properties such as hydrophobicity/hydrophilicity direct protein adsorption on the biomaterial and complement activation of the surface functionalized with these ligands, which are recognized by pattern recognition receptors (PRRs) on DCs and function in a synergistic manner in controlling the immune response to associated antigens [1]. These PRRs include toll-like receptors (TLRs) [2] and C-type lectin receptors [3,4] and function to recognize conserved structures characteristic of pathogens, termed "pathogen associated molecular patterns" (PAMP) [5,6] to induce an immune response to the pathogens. Toll-like receptors and their pathogen-derived ligands are being elucidated and it has been found that exogenous ligands of TLRs include many of the evolutionarily conserved molecules such as lipopolysaccharides (LPS), lipoproteins, lipopeptides, flagellin, double-stranded RNA, and unmethylated CpG islands of DNA [2]. For these reasons TLRs have been considered to essentially act as adjuvant receptors and sustain the molecular basis of adjuvant activity. On the other hand, given the internalization activity of DCs, interactions of DCs with particulate forms of PLGA, polystyrene, and latex have also been investigated [7,8]. Phagocytosis of PLGA or poly(β-amino ester) microspheres showed adjuvant effects or the induction of DC phenotypic changes such as up-regulation of the co-stimulatory molecules CD80, CD86, and CD40 [9–12]. However, in considering the critical roles of other functional or adjuvant receptors in phenotype changes of DCs, the mechanism involved in biomaterial-induced maturation or other functional changes in DCs has not yet been fully elucidated.

In this study the immunobiological functional response of DCs to a variety of biomaterials commonly used in combination products, such as vaccine delivery vehicles or tissue engineered scaffolds, was assessed. The biomaterials used in this study included PLGA as a synthetic polymer and chitosan, alginate, hyaluronic acid (HA), and agarose as natural polysaccharide polymers [13–15]. These biomaterials have been used as scaffolds and cell carriers

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http://dx.doi.org/10.1016/j.actbio.2012.06.006